CHANGES IN THE SODIUM AND POTASSIUM IONS'CONTENT IN THE ARTERIAL VASCULAR WALL UNDER THE INFLUENCE OF THALICTRUM MINUS SSP. ELATUM ALKALOIDS

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Long since known empirical data indicate that a reduced sodium chloride diet accounts for a decrease of blood pressure in a substantial number of hypertonic patients (5, 7, 4, 10, 8). On the other hand, it is well known that hypertonic disease is encountered much more frequently among human groups using salty foods (1). Analogical data, indicating the participation of sodium ions in the pathogenesis of hypertension, although the mechanism of participation remained unclarified, were some of the serious reasons for the introduction of diuretic medicines in the therapy of this particular disease (5). Thirdly, it is proved that the walls of the arterial vessels (of the kidneys) in hypertonic patients display an elevated content of sodium and water per gram tissue (10). A similar elevated content of sodium ions is likewise established in the walls of blood vessels of rats with experimentally produced hypertonia (2). The data reported by a number of authors, indicating that under the effect of continuously infused norepinephrine the level of the sodium in the serum and extracellular fluids is reduced, whereas that of potassium is increased, should also be considered. This phenomenon is related to the infiltration of the sodium into the smooth vascular musculature and to the potassium eliminated therefrom (9). Lastly, the changes in the electrolyte balance of the vascular wall, in accordance with data submitted by various writers, play a definite role in the mechanism of the antihypertensive action of potent means such as reserpine, various diuretic drugs etc.

Taking into consideration the reports cited above and analogical to them literature data on one hand, and on the other — the previously reported by the authors of this paper powerful, practically irreversible under the conditions of acute experiment, hypotensive action of the Thalictrum minus alkaloids (3), we set ourselves the task to investigate their influence upon the content of potassium and sodium ions in the arterial vascular walls of experimental animals.

Material and Method

The experiments were carried out on a series of 32 cats of both sexes, weighing between 1850 and 3350 gr, under urethan narcosis. Extirpation was carried out of one of the femoral arteries in the region of the inguinal fossa, measuring 10—20 mm length, prior to intravenous administration of the

alkaloids in doses 3 and 5 mg per kilogram body weight; it was thoroughl washed in two-fold distilled water, dried on filter paper and weighed wit a torsion balance. The mean weight of these arterial segments amounted t 10—12 mg.

Analogous in size and weight segments were removed from the secon femoral artery 1—3 hours after introduction of the Thalictrum minus alka loids and were accordingly prepared after the same fashion.

Subsequently, the tissue pieces were treated after the method suggeste by V. S. Salmanovich (6), consisting in their burning in the presence of con centrated mineral acid (sulphuric acid). The liquid resulting was diluted i water undergoing two-fold distillation after filtration (which was used als for the washing of the filter paper) until adequate concentration was reached required for the determination of sodium and potassium on flicker photomete „Jouan". The determinations were accomplished on the basis of standar solutions containing 15 mg % K and 330 mg % Na, respectively. The con centrations of these ions in the arterial vascular tissue are likewise presente in milligram percentage.

Results

The results of the investigations are presented in the form of mean va lues with average errors in table 1 and graphically illustrated in figure 1, within confidential limits.

The careful study of the data in table 1 proves that:

1. The potassium ions in the arterial wall are reduced under the influence of the alkaloids introduced. This reduction, however, is not sufficiently significant from statistical viewpoint even in instances of reaching its peak manifestation towards the third hour after venous injection of 5 mg/kg weight of the alkaloids under study.

2. The changes in the sodium ions content are markedly more strongly manifested. Moreover, they get intensified following administration of the alkaloids. At the end of the first hour after injection of both 3 and 5 mg/kg body weight Thalictrum alkaloids, the sodium ions decrease accordingly with 13.3% and 10%. The latter reduction, anyway, is not statistically significant (probability $p \underset{<0.10}{\overset{>0.25}{}}$). The reliability of the reduction at the end of the third hour after giving the alkaloids grows up to undisputable statistically reliable amounts (probability $p = 0.01$). Expressed in percentage, it is equal to 24.9% and 30.5% respectively.

3. The relationship Na^+/K^+ does not exhibit statistically significant deviations towards the end of the third hour following intravenous injection of 3 mg/kg weight, a period in which the reduction of this relationship is most strongly pronounced, reaching 2.10 against 2.56 in controls determinations (probability $p > 0.50$).

Table 1

Data Concerning the Effect of Thalictrum minus Alkaloids Exerted upon Sodium and Potassium Ions'Content in the Arterial Vascular Wall of Cats and the Ratio Na+/K+in Mean Arithmeticals

Experimental background	K^+		Na^+		$\frac{Na^+}{K^+}$
	in mg %	change	in mg %	change	
1	2	3	4	5	6
Control determinations (32)	1.60±0.08	—	4.10±0.16	—	2.56±0.13
Animals injected intravenously with 3 mg/kg alkaloid					
1 hour after inj. (7)	1.46±0.17 $p>0.50$	—8.8%	3.55±0.24 $p<0.25$ $p>0.10$	—13.4%	2.44±0.41
3 hours after inj. (10)	1.47±0.11 $p<0.50$ $p>0.20$	—8.1%	3.08±0.16 $p=0.01$	—24.9%	2.10±0.16 $p>0.50$
Animals injected intravenously with 5 mg/kg alkaloid					
1 hour after inj.	1.40±0.09 $p>0.50$	—12.5%	3.69±0.16 $p<0.02$ $p>0.01$	—10%	2.63±0.23
3 hours after inj.	1.24+0.10 p+0.25	—22.5%	2.85+0.17 $p>0.01$ $p<0.02$	—30.5%	2.30+0.10

Discussion

As the analysis of the results illustrates, a total reduction of the electrolyte content occurs in the walls of a. femoralis of cats under urethan anesthesia, under the effect of the Thalictrum minus alkaloids. Regardless of this finding, the reduction of K^+ should be considered merely as the expression of a tendency in the action of the alkaloids studied, being (the reduction) statistically insignificant. A rather more definite importance for the hypotensive effect of these natural substances is disclosed by the reduction of the sodium ions in the arterial vascular walls. Its reliability, in addition, is increased with the lapse of time following introduction of the alkaloids, in a fashion that while at the end of the first hour it could be assumed merely as a tendency, during the third hour it is a certain fact. In other words, in the arterial vascular walls, exposed to the effect of alkaloids, changes occur inhibiting their capacity of conserving sodium ions chiefly, indispen-

sable for the maintaining of their tone. Thus one of the factors responsible for the maintenance of blood pressure at a determined level — the vascular tone — is substantially inhibited, conditioning on its behalf the fall of pressure.

It should be emphasized, however, that this moment very likely has a bearing not as much on hypotension occurring immediately upon alkaloid

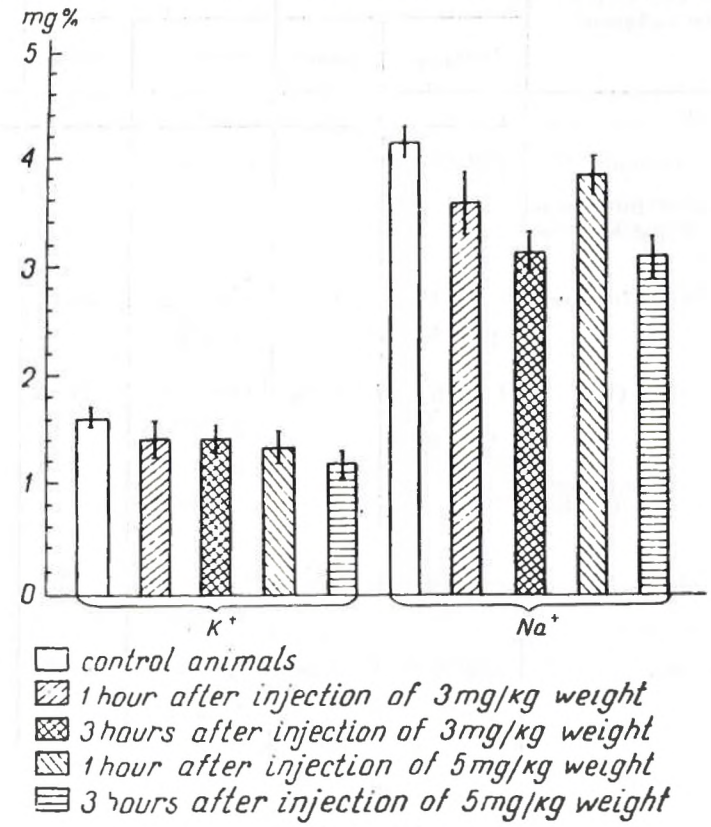

Fig. 1

administration, as for its prolonged maintenance. This conclusion is a consequence of the fact that while the reduction of the content of sodium ions at the end of the first hour after administration of the alkaloids under investigation is at the limit of being statistically significant, at the end of the third hour it becomes unconditionally reliable, i. e. as a phenomenon it gets intensified with passing of time. In addition, this sodium liberating effect of the alkaloids, within the range of 3 and 5 mg per kilogram body weight, does not essentially depend on the dose as, moreover, the hypotensive effect brought about by the quoted quantities of alkaloids does not differ essentially. It seems that it reaches its peak or approximate values at 3 mg/kg body weight and is not furthermore intensified with increasing of the dose (3). The comparative assessment of these two facts on its turn, likewise suggests

the existence of a relationship between the hypotensive effect of the substances investigated and their effect upon the electrolytes in the arterial vascular wall.

As far as the mechanism is concerned by way of which the Thalictrum alkaloids exert their influence upon the electrolyte content of the arterial wall, it must be pointed out that for the time being its accurate determination appears to be rather difficult. Two alternatives are mainly outlined in this respect. On the one hand, it is not excluded that these effects are substantiated by the probable liberation of catecholamines from their stores in the vascular system under the action of the alkaloids introduced (3), and on the other hand, for the time being there are no data justifying the rejection or confirmation of an eventual inhibitory effect upon the adrenal cortex, whose hormones, as well known, are the most closely related to the electrolyte metabolism.

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ИЗМЕНЕНИЯ СОДЕРЖАНИЯ ЙОНОВ НАТРИЯ И КАЛИЯ В АРТЕРИАЛЬНОЙ СОСУДИСТОЙ СТЕНКЕ ПОД ВОЗДЕЙСТВИЕМ АЛКАЛОИДОВ THALICTRUM MINUS, SSP. ELATUM

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РЕЗЮМЕ

Автор исследовал влияние алкалоидов Thalictrum minus, ssp. elatum, отличающихся их мощным, необратимым в условиях острого опыта гипотензивным действием, на содержание йонов калия и натрия в стенке бедренной артерии кошек, находящихся под уретановым наркозом. Обнаруженное снижение количества К-йонов не находится в статистически достоверных пределах, в то время как для Na-йонов оно выраженнее и является статистически достоверным. Особенно сильно выражен этот натрий редуцирующий эффект алкалоидов при исследовании в более поздние часы (3-ий час) после их введения.

Обсуждается значение этих эффектов таликтровых алкалоидов для их гипотензивного действия, а также и вероятный механизм, по пути которого они могли бы реализоваться.